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has proved itself, in comparison with other precipitation or flocculation reactions and with complement-fixation reactions, both highly sensitive and remarkably specific. Moreover, it is easy to perform and rapidly carried out. Whether it should be relied on alone is a matter of opinion. Most workers prefer to use it in conjunction with some form of complement-fixation reaction; this appears to be the ideal, since it would appear that it is rather more sensitive than most forms of Wassermann, especially in treated cases of syphilis; whereas, on the other hand, its specificity has in rare instances been called in question. Further, in the case of spinal fluid the procedure is rather laborious, and it is at least doubtful if it is quite the equal of the best complement-fixation reactions. It should be pointed out that the author has not attempted to produce the most sensitive test possible, but has aimed at a somewhat conservative one in order to attain the maximum of specificity. When sensitiveness is the principal object, the presumptive procedure should be adopted. It is doubtful how far the laborious and complicated procedure of standardising an antigen is necessary; where the reaction is to be used alone it is certainly necessary, but when it is used in parallel with some other method, either precipitation or complement-fixation, it does not seem to be so essential, though in any case it is wise to compare a "home-made" antigen with standard antigen before taking it into routine use. Fortunately the latter can now be purchased in this country, though it is somewhat expensive.

T. E. O.

SERUM DIAGNOSIS BY COMPLEMENT-FIXATION. By Professor Kolmer. Pp. xix + 583. 65 Figures. Messrs. Ballière, Tindall and Cox. 1929. Price 31s. 6d. net.

(Second Notice.)

"THIS book," as stated by the author, "is essentially a summary of the clinical and laboratory investigations which I have made . . . in serum diagnosis by complement-fixation, not only in syphilis, but likewise in the wide field of the bacterial, protozoal and metazoal diseases of human beings and the lower animals, and in the identification of blood and seminal stains, the detection of meat and milk adulterations and other soluble albumins."

Part I. deals with the underlying principles of serum hæmolysis and complement-fixation.

Hæmolysins, also known as sensitisers and amboceptors, may be divided into *natural* and *immune*. The former are of importance not only in relation to blood transfusion but also in complement-fixation, since some workers have relied on these in performing modifications of the Wassermann reaction; they also sometimes play a part in the ordinary Wassermann test, since they may be present occasionally in such comparatively large amounts as to tend to produce a falsely negative reaction. Immune hæmolysins, on the other hand, are produced by injecting an animal with the erythrocytes of an unrelated species, and it is this variety which is employed in carrying out the Wassermann reaction; it is highly specific for its corresponding or homologous antigen of erythrocytes. The active antigenic constituent of erythrocytes appears to lie mainly in the protein of the stroma,

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whilst the hæmoglobin and lipoids play a very small part in hæmolysin production. Serum hæmolysins are relatively stable substances, resistant to heat, age, chemical agents and desiccation. The author defines them as antibodies capable of uniting with their homologous erythrocytes and rendering them sensitive or susceptible to the lytic effects of complement, but points out that their nature is somewhat uncertain ; probably they are proteins belonging to either the pseudo-globulin or euglobulin fraction of serum, and not enzymes.

Complement, on the other hand, is very susceptible to physical agencies. It is defined as "a substance present in both normal and immune sera which produces lysis of sensitised antigen." Its nature is obscure, but the author gives a summary of evidence tending to show that it is an enzyme, stating that in his opinion "serum hæmolysis is an intra-corpuscular enzymic reaction in which the hæmolysin renders the corpuscles susceptible to an enzyme in the complement and resulting in the digestion of stroma sufficient for the release of hæmoglobin."

In a discussion on the phenomenon of complement-fixation, the author points out that the Wassermann reaction depends on a biologically non-specific fixation, though for practical purposes it may be regarded as specific, and shows how by complement-fixation if an antigen is known an antibody may be detected, and if an antibody is known an antigen may be detected.

Turning to complement-fixing antibody, the author concludes that it lies in the globulin fraction and deals with its properties and probable immunological nature.

Antigens are defined as substances which cause the production of specific and non-specific antibodies ; in Wassermann antigens lecithin appears to be the most important single active constituent, and its activity is increased by cholesterol or soaps, also by alcohol.

As regards the mechanism of complement-fixation which is discussed at length, the author concludes that in the Wassermann when "extract" and syphilitic serum are brought together there is a change in the menstruum capable of inactivating the complement enzyme.

A whole chapter is devoted to anticomplementary action, the nature of which is unknown. In practice, it is only of importance when the serum or fluid to be tested fixes complement alone. Most frequently this is due to contamination or a marked degree of hæmolysis, neither of which should occur under well-regulated conditions. Most antigens tend to be anti-complementary, but the degree of this should be low if a satisfactory technique is followed.

The whole subject of the four principal ingredients of the Wassermann reaction, hæmolysin, antigen, antibody and complement, is little understood. None has been isolated, and their nature is unknown. The author has presented this part of his subject most fully, giving his own theories with moderation and discussing those of others.

Part II. deals with the principles of complement-fixation technique, including glassware, saline, hæmolytic system (including hæmolysin and red cells), complement, antigen and serum to be tested.

He prefers to use a separate pipette for each serum tested. This, no doubt, is the ideal, but since there can be no possible danger in using the same one if well rinsed out between any two successive sera, whilst the use of a single pipette involves a very considerable saving of time, it would appear to be a counsel of perfection. The influence of excess

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of natural anti-sheep hæmolysin in serum in the W.R. is stressed, and the author's method of removing it is given. This is a very real danger in the production of "false negatives" in many forms of technique, but may be largely eliminated by the employment of excess of hæmolysin in making up the hæmolytic system, which involves far less labour than absorption from each serum with sheep's cells. The author chooses the anti-sheep system, absorbing the natural anti-sheep hæmolysin, giving his reasons.

For cell suspensions, sheep's cells are recommended. These need not be counted, as slight variations in concentration have little effect on the reaction provided the same suspension is used throughout.

Complement is dealt with at considerable length, especially in regard to fixability and hæmolytic activity, and the author concludes that a mixture of several complements is superior in many ways to a single one. He rightly emphasises the advisability of employing young healthy well-fed guinea-pigs; various methods of preserving complement are described—freezing solid being perhaps the simplest and best.

Hæmolysin is obtained by injecting rabbits intravenously with washed sheep-cells; there can be little doubt that the rabbit is the animal of choice, and the use of most others is to be deprecated.

A full discussion is given on the adjustment of the hæmolytic system and titration of hæmolysin and complement. The author comes to the conclusion that the best and most sensitive reactions are obtained when the tests are conducted with plain corpuscles and two units of hæmolysin added separately. No doubt this is correct, but it is problematical if the gain in sensitiveness counterbalances the large amount of extra labour involved. Antigen is probably the most important single factor influencing the results of the test; it is also the most variable from worker to worker, and this probably accounts for the variability of results in different laboratories. Human or ox heart, dried, is considered the best source, and the author employs an alcoholic extract to which he adds the acetone insoluble lipoids and 0.2 per cent. cholesterin. Antigens for bacterial complement fixation tests are given a chapter to themselves. Most of the numerous methods of preparing them are described and criticised, and many interesting points are brought out; in general, suspensions of dried and ground organisms or whole fresh organisms in saline furnish the best antigens; heating to 80° or more seems to improve their quality. The whole subject is a vast one, since it would appear that no one method is applicable to all bacteria. A volume might easily be devoted to the subject.

Turning to the test itself, the author discusses the influence of heat on the serum to be tested, the order of adding the ingredients (he prefers to add complement last), the influence of temperature and the duration of the primary incubation, the secondary incubation and the time of reading results. The period of the primary incubation varies greatly from worker to worker; the author employs one of sixteen to eighteen hours at 6° to 8° C., followed by ten to fifteen minutes in a water-bath at 38° C. There can be little doubt that the long ice-box fixation increases the sensitiveness of the test, but many fear that it leads to occasional non-specific results. The time of reading reactions is of the greatest importance, and this is where the experienced serologist has the advantage over the inexperienced. More delicate results will be

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obtained if reading is carried out individually on each serum of a batch than if all are read together at the end of a specified time. On the other hand, if read too soon, non-specific weak positives will occur. The author therefore recommends that reading should be carried out ten minutes after complete hæmolysis of the antigen control.

Part III. is devoted to a minute and detailed description of the author's own test, for which reference should be made to the original. This includes, not only the test as applied to syphilis, but also to bacterial or protozoal diseases, and for a number of other purposes such as the identification of blood stains.

Special attention should be directed to Chapter XXX., where the author discusses such subjects as discrepancies in the Wassermann reaction, the advantages and disadvantages of standardisation and sources of error in the reaction. A valuable step towards standardisation would be the adoption of a standard antigen prepared, titrated and distributed by central laboratories.

Part IV. is devoted to the clinical application of complement-fixation tests. As regards specificity, the Kolmer test is claimed to give positive results in only one disease other than syphilis, viz., yaws. All the host of diseases such as typhus, typhoid, pneumonia, scarlatina, tuberculosis, malaria, leprosy, diabetes, nephritis, are definitely excluded. Coming from such an authority this is extremely comforting. The average clinician reads this list in text-books, and, when he receives a positive report which does not tally with the clinical findings, wonders which of these diseases his patient is suffering from. There can be little doubt that various workers at different times have reported an occasional positive in a number of diseases, and in this way a long list of diseases which give false positive reactions has been evolved. That yaws should give a positive W.R. is not surprising when one considers that the causal organism is microscopically indistinguishable from that of syphilis, that many of the manifestations of the two diseases are similar, and that both are amenable to the same drug. For the value of the Kolmer test in the diagnosis and treatment of syphilis, the reader should refer to the original. Suffice it to say, that this test appears to be equal, if not superior, to any complement-fixation test for syphilis.

The value of complement-fixation in other diseases is very debatable. Most of them can be more easily diagnosed in other ways, but in certain, such as gonorrhœa and echinococcus disease, to mention only two, it may be of great value.

There can be little doubt that the Kolmer test for syphilis combines a high degree of sensitiveness with remarkable specificity. On the other hand, it is extremely laborious and time consuming. The point at issue is whether the gain in accuracy more than counterbalances the extra labour. Probably where great numbers of tests are to be carried out in large central laboratories under almost perfect conditions by highly skilled workers, the Kolmer test is most applicable; but where relatively small numbers of tests are dealt with, a simpler and less laborious technique is to be preferred.

Professor Kolmer is to be congratulated on the production of what is probably the best book yet produced on the subject of complement-fixation in all its aspects. No detail is omitted, and the whole complicated subject is set out with the utmost clearness. The book should

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be read by all who practise complement-fixation, for whom it is primarily written, but the clinician will find much to interest and instruct.

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SEX AND ITS MYSTERIES. By George Ryley Scott, F.R.A.I., F.Ph.S., F.P.C.(Lond.), F.Z.S. Cr. 8vo. Pp. iv + 198. Price 10s. 6d. net. London: John Bale, Sons & Danielsson, Ltd., 1929.

IT is said, in the very complete account of this little book, so agreeably furnished to the "indolent reviewer" by the thoughtful publishers, that it is a most valuable contribution to the literature of sex. The author, we are told, treats "exhaustively" every phase, and discusses "scientifically, effectively and enlightenedly," every one of the problems of "sexual physiology." "Infinite skill, courage and distinction" are displayed, and "here lies the uniqueness of the book." It is the work of one of the "most daring and advanced writers of the age"—a "writer of brilliance and distinction" who brings an "encyclopædic knowledge of sexual physiology and psychology" to his task, and who has not only "exploded a farrago of popular fallacies and myths" but has "divulged the whole truth about sex." Nay, more, he has "faced squarely" the "facts in all their starkness"; he has handled them "without gloves." It is impossible, we learn, to indicate with pretence to completeness "the tremendous scope and variety of the book's contents," but "resolutely, skilfully, entertainingly, logically, pitilessly it draws aside the curtains that wholly or partially conceal the mysteries of sex." Beliefs are "ruthlessly demolished," and disturbing facts "hitherto unknown to the lay public are unburied and explained." All this, too, for eleven shillings, post free, within the compass of one hundred and ninety-eight small pages!

In face of such stupendous qualities a reviewer, at all times conscious of his responsibility, must feel himself deplorably inadequate to the occasion. He can only draw attention to the characteristics of the work, as proclaimed by the publishers, and thereafter content himself with noting some of the features that have given interest to the task of perusal.

In the first place, we should note that the author, "at the risk of being dubbed old-fashioned," asserts that the success, in recent times, of what he calls the wide and universal conspiracy to keep the young of both sexes in ignorance of sexual matters as long as possible, "was all to the good." Rob the sexual act and woman of their mystery, reduce woman and the sexual act to the level of physiological entities (he maintains), and "you destroy at the same time the only distinction between the intercourse of two lovers and that of the *roué* and the prostitute." So much being made clear he announces, two or three pages further on, that he is attempting to "pull wholly aside the curtains that still partially conceal" the mystery of sex and woman.

This he proceeds to do, with infinite gusto. There is no doubt about the unusual quality of the writing: the nice derangement of epitaphs leaves Mrs. Malaprop gasping from the word "go." Hypotheses are "smashed to splinters," and "old theories" to "fragments"; while the "gates of wrath" would be "with a vengeance let loose" upon medical men who would suggest coitus apart from marriage, in